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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/997,573 | 11/15/2001 | Avi J. Ashkenazi | P2730P1C45 | 3279 |
| 9157 | 7590 | 04/06/2004 | EXAMINER | |
| GENENTECH, INC. 1 DNA WAY SOUTH SAN FRANCISCO, CA 94080 | | | HAMUD, FOZIA M | |
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1647

DATE MAILED: 04/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/997,573

Applicant(s)

ASHKENAZI ET AL.

Examiner

Fozia M Hamud

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 119-131 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 119-131 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicant's preliminary amendment canceling claims 1-118 and adding new claims 119-131, filed on 15 November 2001 is acknowledged.

Thus claims 119-131 are pending and under consideration.

Priority:

2a. Based on the information given by Applicants and an inspection of the patent applications, the Examiner has concluded that the subject matter defined in this application is not supported by the disclosure in application serial no. 09/941,992 filed on 28 August 2001, because, although the claimed polypeptide (PRO1375) is disclosed as SEQ ID NOs:418, in application 09/941,992, none of the parent applications provide a specific and substantial asserted utility or a well established utility for the claimed invention. Accordingly, the subject matter defined in claims 119-131, is afforded an effective filing date of 11/15/2001, which is the filing date of the current application.

Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s) of any parent application filed prior to 11/15/2001, which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to 11/15/2001.

Specification:

3a. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is

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requested in correcting any errors of which applicant may become aware in the specification.

Information Disclosure Statement:

4a. References A1 and A2, cited on the PTO-1449 form submitted by Applicants on 31 May 2002 have not been considered, because they do not comply with 37 CFR 1.98(a)(2) requirements, since they fail to identify each publication by author and publication date. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Claim Rejections - 35 U.S.C. § 101/112:

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5a. Claims 119-131 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Claims 119-131 of the instant invention are directed to an isolated polypeptide of SEQ ID NO:418. The specification designates the polypeptide of SEQ ID NO:418, as PRO1375, and describes it as being a human polypeptide that comprises 198 amino acid residues, (figure 300). Although the specification discloses the amino sequence of the claimed PRO1375, however, specification does not disclose any information regarding physiologic activity or functional characteristics of the PRO1375 polypeptide.

Example 151 on page 525 of the instant specification discloses that the claimed PRO1375 has tested positive in stimulatory mixed lymphocyte reaction assay, (MLR) assay. However, the ability of a protein to stimulate lymphocyte proliferation in this assay does not support a specific and substantial utility for the claimed invention. The ability to stimulate or inhibit lymphocyte proliferation in the MLR assay is an artificial in vitro system and does not provide for what specific conditions or for which specific diseases the claimed invention would predictably function. The assertion that the claimed invention could be useful for the treatment of conditions where the enhancement of the immune response would be beneficial (page 525, lines 2-6) is not specific since there are many such conditions, and it is not predictable of which conditions the claimed invention may function, if any.

Mixed lymphocyte culture (MLC, a.k.a. MLR)) is a special case of antigen stimulation in which T lymphocytes respond to foreign histocompatibility antigen on unrelated lymphocytes or monocytes. MLR is a functional assay of cellular response to stimulatory determinants associated predominantly with HLA class II molecules.

The MLR assay is a measure of alloreactivity of one individual to another individual, rather than a general measure of immune function. This reactivity is governed by the antigenic disparity between the two individuals who are being compared in the assay. Depending on the individuals being tested, the MLR may indicate stimulation if they are HLA-disparate or the MLR may indicate no stimulation if the individuals are HLA-identical. The ability of the claimed invention to stimulate proliferation in the MLC assay may not be a general stimulus to lymphocyte

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proliferation, but rather a reaction to one of the MHC antigens on the responder cell.

The instant specification fails to provide sufficient detail of the assay, which was performed and fails to provide any data whatsoever in order for one of ordinary skill in the art to evaluate the conclusion that lymphocyte proliferation was stimulated by the claimed invention.

Furthermore, there is known inherent variability of individual cellular responses from day to day, which would clearly dictate the need for internal controls. The specification indicates that CD4-IgG was used as a control, but it is not clear how this would control for background stimulation or provide for a measure of maximal stimulation. Lastly, the specification fails to provide any data or evidence of the results of the assay, therefore, one of ordinary skill in the art cannot evaluate the conclusion. The specification states that "positive increases over control are considered positive", however, this does not indicate that statistical significance must occur for determination of a positive result in the assay. In conclusion, the results of the MLR assay do not support a specific and substantial utility for the claimed invention because the assay is not predictive of immune response in general, and one of ordinary skill in the art would not expect a stimulatory effect in the MLR assay to correlate to a general stimulatory effect on the immune system, absent evidence to the contrary. Furthermore, there is no information regarding the correlation of the MLR results to any real-life diseases. There is no information regarding what subsets of immune responses, immune cell types etc. are targeted by compounds with activities in MLRs.

Instant specification also discloses that PRO1375 tests positive as a stimulator of glucose and/or FFA uptake assay, (see page 530, lines 13-14). The specification further asserts that polypeptides that test positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either stimulation or inhibition of glucose uptake would be beneficial, (page 530, lines 3-6). However, this assay appears to be prophetic, and the specification offers no guidance regarding how this assay is beneficial in treating any disorder. The specification provides no data of glucose and/or FFA uptake. There is no evidence of a link between this protein and any of the diseases listed on page 530 of the instant specification. Therefore, one of ordinary skill in the art would not know how to use the claimed polypeptide to treat any disorder.

Thus, since instant specification provides no information regarding the physiological significance or any conditions that involve the polypeptide of SEQ ID NO:418, (PRO1375 polypeptide), said polypeptide, lacks specific and substantial asserted utility or a well established utility.

5b. Claims 119-131 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantially asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. No biological activity was assayed or determined for the PRO1375 polypeptide. Therefore, there is no specific and substantial asserted utility or well established the PRO1375 polypeptide. Although the specification describes the structure of PRO1375 polypeptide, the skilled artisan would not know how to use said PRO1375 polypeptide, because Applicants do

not provide any information regarding biological activity or physiological characterization of said polypeptide. Instant specification also fails to establish a correlation between the polypeptide of the instant invention and a disease state.

5c. Claims 119-128 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Should Applicants establish an activity for the polypeptide of SEQ ID NO: 418, instant specification would still fail to adequately describe and enable an isolated polypeptide comprising an amino acid sequence that is at least 80%, 85%, 90%, 95% or 99% to the polypeptide of SEQ ID NO:418. Claims 119-123 are drawn to a polypeptide having at least 80%, 85%, 90%, 95% or 99% sequence identity with a particular disclosed sequence. The specification does not provide any particular conserved structure, or other distinguishing features which would enable a polypeptide having at least 80%, 85%, 90%, 95% or 99% to the polypeptide of SEQ ID NO:418 that would retain the activity of the polypeptide of SEQ ID NO:418. Claims 119-124, 126, 128 are drawn to the polypeptide of SEQ ID NO:418, lacking its associated signal peptide, however, the specification does not disclose which residues of the polypeptide of SEQ ID NO:418 represent said signal sequence. Also claims 119-124, 127 are drawn to an amino acid sequence of the extracellular domain of the polypeptide of SEQ ID NO:418. However, the specification does not provide written description for said extracellular domain, since it does not teach which residues of the polypeptide of SEQ ID NO:418

represent said extracellular domain. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement

that it is part of the invention and reference to a potential method of isolating it. The compound itself is required.

Therefore, only the isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 418, but not the full breadth of the claims meet the written description provision of 35 U.S.C. §112, first paragraph.

5d. Claims 119-131 are ejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 119-131 are rejected, because the claims are drawn to a "cDNA deposited under ATCC accession number 203115". It is apparent that the cDNA is required to practice the claimed invention. As such said cDNA must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If the cDNA is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of this cDNA.

The specification, provides an ATCC accession number for the claimed cDNA, however, the specification lacks complete deposit information for the deposit of the cDNA. If a deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would

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satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that (a) during pendency of the application, access to the invention will be afforded to the Commissioner upon request, (b) all restrictions upon availability to the public will be irrevocable removed upon granting of the patent, © the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer, (d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807) and (e) the deposit will be replaced if it should ever become inviable.

Claim rejections-35 USC § 102(b):

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6a. Claims 119-125, 129-131 are rejected under 35 U.S.C § 102(b) as being anticipated by MILLENNIUM BIOTHERAPEUTICS INC, (MILL), (WO 00/18904 June/2000); GENENTECH INC. (GETH), (WO 99/63088, September/1999); INCYTE

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(INCY), (WO 00/00610, June/2000); SAGAMI CHEM RES CENT (SAGA), (WO 00/00506, June/2000) .

Each of references, MILL, GETH, INCY and SAGA, discloses an isolated polypeptide that shares 100% amino acid sequence identity to the amino acid sequence of the polypeptide of SEQ ID NO:418, recited in claims 119-125, 129-131 of the instant application . See attached copies of the comparison of SEQ ID NOs:418, claimed in the instant invention and the sequences of the references (SEQUENCE COMPARISON 'A', 'B', 'C', 'D'). Regarding claim 129, it is understood that the deposited sequence encodes the polypeptide of SEQ ID NO:418, therefore, since the polypeptide disclosed by each of the above references shares 100% identity to the polypeptide of SEQ ID NO:418, these references also anticipate claim 129. With respect to claims 130 and 131, each of the cited references also discloses a chimeric or fusion protein comprising its polypeptide and a heterologous polypeptide, (see for example the MILL reference, pages 65-68).

Therefore the MILL, GETH, INCY and SAGA references, all anticipate the instant claims 119-125, 129-131 in the absence of any evidence to the contrary.

Claim rejections-35 USC § 102(a):

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

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6b. Claims 119-125 and 129 are rejected under 35 U.S.C § 102(a) as being anticipated by HELIX RES IST. (HELI), (EP 1130094, September/2001).

HELI reference discloses an isolated polypeptide that shares 100% amino acid sequence identity to the amino acid sequence of the polypeptide of SEQ ID NO:418, recited in claims 119-125 and 129 of the instant application . See attached copies of the comparison of SEQ ID NOs:418, claimed in the instant invention and the sequences of the references (SEQUENCE COMPARISON 'E'). Regarding claim 129, it is understood that the deposited sequence encodes the polypeptide of SEQ ID NO:418, therefore, since the polypeptide disclosed by HELI reference shares 100% identity to the polypeptide of SEQ ID NO:418, this reference also anticipates claim 129.

Therefore the HELI reference anticipates the instant claims 119-125 and 129 in the absence of any evidence to the contrary.

Conclusion:

7. No claim is allowed.

Advisory Information:


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday, Thursday-Friday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary L Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Fozia Hamud
Patent Examiner
Art Unit 1647
30 March 2004


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SUPERVISORY PATENT EXAMINER
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